Effects of Chlorpromazine and D-Lysergic Acid Diethylamide on Sex Behavior of Male Rats.* (25532)

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The effects of psychotropic drugs on sex behavior are of interest to understanding of drug action as well as physiological mechanisms underlying sex behavior. Soulairac and Coppin-Monthillaud(1) and Zimbardo and Barry(2) found that injection of caffeine in the male rat shortened latency to first copulation and increased rate of copulation. Furthermore, injection of 1 mg/kg of chlorpromazine prolonged latency to first copulation and decreased rate and frequency of copulation(2). The present report deals with effects of chlorpromazine and LSD-25 on sex behavior of male rats.

Method. Twelve 150 day old Sprague-Dawley male rats were kept in individual cages on 12-hour light and 12-hour dark cycle and tested during dark half of cycle. Females used as stimulus partners were brought into estrus by estrogen and progesterone† (3). They were placed with an active, nonexperimental male, and only those showing full behavioral heat were used in the tests. During tests animals were observed in semicircular observation cages 20″ in diameter with glass front. At start of test the male was allowed 2 minutes in the cage before female was introduced. If the male did not copulate within 15 minutes, and if it failed to reach ejaculation within 30 minutes, the test was terminated. Animals were selected from a larger group of males on the basis of achievement of ejaculation within 30 minutes. The mating pattern of the male(4) consists of a series of copulatory mounts with brief intromission lasting approximately ⅓ second. Each copulation is separated from the next by average interval of 45 to 60 seconds. After 8 to 15 copulations, ejaculation occurs, followed by 5 minutes, during which the male engages in no sexual activity. The following measures were made on each test: a) Copulation latency: time in seconds from introduction of female to first complete copulation. b) Number of copulations preceding ejaculation: number of mating responses resulting in intromission. c) Number of incomplete copulations: responses with mounting of female and pelvic thrusting without intromission. d) Ejaculation latency: time in seconds from first copulation to ejaculation. e) Recovery period: time in seconds from ejaculation to next copulation. Trials 1 through 10 were spaced 72 hours apart, and trials 10 through 15 96 hours apart. Each subject was allowed 1 ejaculation/trial. Before receiving any drug, each of the 12 inexperienced males underwent 4 consecutive training trials to obtain consistent, stable behavior(5). In Table I the drug, dosage conditions, and number of animals injected are listed for each trial beginning with trial No. 5. Chlorpromazine HCl‡ was injected intraperitoneally in dose of 2.5 mg/kg at concentration of 6.25 mg/cc, and LSD-25 in doses of 130 and 200 γ/kg at concentration of 1 mg/cc (1 mg = 1000 γ). Placebos consisted of equivalent volume of distilled water injected as the drug on the following drug trial. Dosage of 2.5 mg/kg of chlorpromazine depresses food intake in the rat(6). Dosage of 130 γ/kg of LSD and daily injection of this dose for 3 days between trials 13 and 14 was used to determine whether the effects of LSD on sex behavior show tolerance. Freedman, Aghajanian, Ornitz, and Rosner(7) have shown that this dosage schedule produces tolerance to impairment of rope-climbing in rats due to LSD.

Results. Both chlorpromazine and LSD reduced the number of copulations preceding

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‡ Chlorpromazine hydrochloride was supplied through the courtesy of Smith, Kline & French and LSD-25 through courtesy of Sandos Lab.

TABLE I. Experimental Conditions and Group Behavior for Each Trial in Terms of Observed Parameters.

Trial No.	No. of subjects	Drug and dosage	Trial No.	No. of subjects	Drug and dosage
5	12	placebo	10	12	placebo
6	"	chlorpromazine, 2.5 mg/kg 30 min.	11	11	LSD, 200 γ/kg 5 min.
			12	12	placebo
7	"	placebo	13	"	LSD, 130 γ/kg 5 min.
8	"	"		daily inj. of	LSD, 130 γ/kg for 3 days
9	"	chlorpromazine, 2.5 mg/kg 30 min.	14	12	LSD, 130 γ/kg 5 min.
			15	"	placebo

Median copulation latency (sec.)	Mean No. copulations preceding ejac.	Mean No. copulations/min.	Mean No. copulatory attempts	Mean ejac. latency (min.)	Mean recovery period (min.)
20	13.5	1.21	7.4	11.2	6.3
45	9.8	.80	7.1	12.2	7.3
10	13.1	1.38	6.5	9.5	5.7
15	"	1.95	6.6	6.7	6.3
"	8.7	1.55	6.3	5.6	6.6
"	14.0	1.71	7.3	8.2	5.7
10	6.2	.91	5.2	6.8	5.5
"	11.6	1.71	3.4	"	5.1
"	8.2	1.75	6.4	4.7	5.2
"	9.2	2.24	5.8	4.1	4.7
15	11.8	1.47	5.1	8.0	5.0

ejaculation. Group performance of those that copulated and ejaculated is shown in Table I for each trial. Median rather than mean latency to the first copulation is presented as a better measure of central tendency because of skewed distribution of latencies. By comparing the score of each animal on a drug trial with his score on the preceding placebo trial, it was possible to use each animal as his own control. Only scores of those subjects that achieved ejaculation within 30 minutes on both drug trial and preceding placebo trial are included in the statistical evaluation (Table II). All 12 subjects achieved ejaculation within 30 minutes on all placebo trials. In trial 11 with LSD, 5 subjects failed to copulate, and in trial 13 with LSD 2 subjects failed to copulate. The high incidence of failure to copulate on trials 11 and 13 appeared to reflect the severity of motor disturbance induced by acute doses of LSD.

Reduction in number of copulations preceding ejaculation by LSD did not follow the pattern of tolerance described for impairment of rope-climbing by LSD(7). On trial 14, after tolerance to LSD had been presumably established, subjects still showed a low number of copulations preceding ejaculation, although they did not display the severe motor incoordination characteristic of acute effects of LSD present in trials 11 and 13.

The number of copulations/minute, or rate of copulation, was significantly reduced only on the first trial with chlorpromazine, trial 6. The low rate of copulation on trial 11 and high rate of copulation on trial 14 are sug-

TABLE II. Significance of Difference between Mean No. of Copulations Preceding Ejaculation on Each Drug Trial and Preceding Placebo Trial.

Drug tested	Trials compared	Diff. between mean No. copulations preceding ejac.	N	t	p
Chlorpromazine, 2.5 mg/kg	5-6	3.7	11	2.6	.05
Idem	8-9	4.4	12	4.0	.01
LSD-25, 200 γ/kg	10-11	7.0	6	6.6	"
LSD-25, 130 γ/kg	12-13	3.6	10	5.1	.001
Idem tolerance	12-14	2.4	12	4.6	"

gestive of treatment effects but do not approach statistical significance.

Summary and conclusions. Effects of chlorpromazine and LSD-25 on sex behavior of 12 male albino rats were studied. Chlorpromazine at 2.5 mg/kg injected 30 minutes before trial and LSD at both 200 γ/kg and 130 γ/kg injected 5 minutes before trial, reduced the number of copulations preceding ejaculation. Reduction in number of copulations by LSD did not follow the pattern of tolerance described for impairment of rope-climbing by LSD. Rate of copulation on the first trial that chlorpromazine was given was significantly slowed.

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Water, Neutral Fat and Solids of Adipose Tissue.* (25533)

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It is variously stated that water accounts for from 5 to 30% of the weight of adipose tissue(1). The amount of water associated with fat is a variable which may influence values obtained for lean body mass and total body fat calculations when these parameters are estimated from densitometric or from total body water measurements(2). In this connection the question arises, does adipose tissue increase in size and weight as the result of addition of both water and neutral fat or are neutral fats incorporated into adipose tissue without inclusion of significant amounts of additional water? Since adipose tissue can make up from about 5 to 50% of an individual's total body weight, it is of interest to determine the factors which may influence the variability of adipose tissue composition. This report presents the results of an investigation in which relationships among neutral fat, solids and water in adipose tissue were studied.

Methods. Twenty-four adult male Sprague-Dawley rats were subjected to a cold environment (4-8°C) from 23 to 26 days; 12 control animals were maintained at room temperature (22-24°C). In both groups water and food (Purina Dog Chow) were given *ad lib.* Peri-renal adipose tissue was removed as completely as possible from etherized, exsanguinated, adult white male Sprague-Dawley rats. Water was estimated by weight difference after drying *in vacuo* (40-60 mm Hg subatmosphere pressure) at 38°C for 48 hours. Neutral fat was estimated after extraction with ethyl ether. The weight of the dry, defatted residue represents solids present in the adipose tissue.

Results. The weight of peri-renal adipose tissue in experimental and control animals fluctuates as a function of individual variation and/or as the result of exposure to low temperature for prolonged periods. As weight of the adipose tissue increases, the percent water decreases exponentially, whereas the percent neutral fat increases exponentially (Fig. 1). Large samples of adipose tissue contain about 5% water and 95% neutral fat whereas in smaller samples there may be 30-40% water, and only 50-60% neutral fat.

In an attempt to study these relationships further, data from both experimental and con-

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